UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/786,400	02/24/2004	Alexander William Oxford	56476-DIV2 (71661)	2879

21874 7590 05/12/2005

EDWARDS & ANGELL, LLP
P.O. BOX 55874
BOSTON, MA 02205

EXAMINER	
TRUONG, TAMTHOM NGO	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 05/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/786,400	OXFORD ET AL.	
	Examiner	Art Unit	
	Tamthom N. Truong	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *43-48,51 and 52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-48,51 and 52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/964,260.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2-24-04*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's preliminary amendment of 2-24-04 is acknowledged and entered.

Claims 1-42, 49 and 50 are cancelled.

Claims 43-48 have been amended. Claims 51-53 have been added. Thus, pending claims are 43-48, 51 and 52.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claim 46 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 46 recites the limitations of "*each of R^1 and R^2 represents a C_{1-6}alkyl; R^1 and R^2 are the same as each other*" (the same recitation for R^7 and R^8). Said limitations have indefinite metes and bounds because it is unclear if the second limitation is a requirement or an alternative. Another words, if R^1 were *methyl*, would R^2 also be *methyl* as well? Or, would R^2 be *ethyl* or *propyl*?

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Enablement (for "prevention"):** Claims 43-48, 51 and 52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Claims 43-45 recite a "*method for the ...**prevention***" which does not have enablement in terms of patient's profile, preventive dosage, onset and duration of prevention. Without such a protocol, a skilled clinician would have to carry out undue experimentation to use the claimed compound in the prevention of any intended disease.

3. **Scope of Enablement (for compounds and diseases):** Claims 43-48 and 51 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating asthma or COPD using compounds of formula I wherein X is CR^3R^4, does not reasonably provide enablement for the same method but using compounds of formula I wherein X is OCH_2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

(1) The breadth of the claims;

(2) The amount of direction or guidance presented;

(3) The state of the prior art;

(4) The relative skill of those in the art;

(5) The predictability or unpredictability of the art;

(6) The quantity of experimentation necessary;

[See ***Ex parte Forman***, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also ***In re Wands***, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The breadth of the claims:

Claim 43 recites: "*A method for the treatment or prevention of a disease in a mammal where a phosphodiesterase isoenzyme inhibitor and/or a bronchodilator...*" which encompasses the treatment or prevention of many diseases such as: *asthma, allergic asthma, hay fever, allergic rhinitis, bronchitis, chronic obstructive pulmonary disease (COPD), adult respiratory distress syndrome (ARDS), and cystic fibrosis, atopic dermatitis, psoriasis, ocular inflammation, cerebral ischaemia, and auto-immune diseases.* Not only the scope of claim 43 is broad in term of diseases, but also in term of the compounds represented by formula I.

Claim 44 recites: "*A method for the treatment or prevention of asthma...*" which is not broad in term of disease, but is still broad in term of the compounds represented by formula I.

Claim 45 recites: "*A method for the treatment or prevention of chronic obstructive pulmonary disease (COPD)...*" which is not broad in term of disease, but is still broad in term of the compounds represented by formula I.

Claims 46-48 and 51 depend on claims 43-45, and thus, carry the same broad scope.

The amount of direction or guidance presented: The *in-vitro* assay shows an IC_{50} value (for the inhibition of phosphodiesterase isoenzyme (PDE)) of the compound of Example 1 – a compound of formula I in which X is CR^3R^4. The *in-vivo* assay shows the compound of Example 1 could protect against *brochospasm*, or inhibit "*the recruitment of eosinophils to the lungs*". Such a data only confirm that a compound of formula I in which X is CR^3R^4 could treat asthma or COPD. However, said finding cannot be extrapolated to the treatment of other diseases such as: atopic dermatitis, psoriasis, ocular inflammation, cerebral ischemia, cystic fibrosis, etc. because there is no *in-vivo* test on the skin, eyes, brain, etc. Also, the activity of a compound of formula I wherein X is CR^3R^4 cannot be extrapolated to those of formula I wherein X is OCH_2 since there is no structural similarity between the two tricyclic systems. Thus, the specification fails to provide sufficient enablement for the intended scope.

The state of the prior art: As evident by the references cited on the IDS and PTO-892, there is no equivalent teaching for a tricyclic system in which X is CR^3R^4, and a tricyclic system in which X is OCH_2. Therefore, the state of the art does not overcome the deficiency in the enablement provided by the instant specification.

The relative skill of those in the art: Even with the advanced training, the skilled clinician would have to engage in undue experimentation to establish data that would adequately support the treatment of asthma or COPD using a compound selecting from a large genus of formula I which has two different tricyclic cores depending on X. Such a task would require a tremendous amount of effort, time and resources.

The predictability or unpredictability of the art & The quantity of experimentation necessary: The pharmaceutical art has been known for its unpredictability due to various conflicting pathways, or biological factors that are sometimes genetically unique to individuals. In the instant case, the specification only shows evidence for the treatmen of asthma or COPD using a compound of formula I in which X is CR^3R^4. However, said evidence does not adequately guide the skilled clinician in selecting the compound of formula I in which X is OCH_2 to treat the same diseases or other diseases that are related to phosphodiesterase isoenzyme. Thus, with such a limited teaching, the skilled clinician would have to carry out undue experimentation to use the claimed compounds in the methods recited in claims 43-48 and 51.

No pending claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 571-272-0676. The examiner can normally be reached on M-F (10:00-6:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Tamthom N. Truong
Examiner
Art Unit 1624

4-27-05

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600